haloperidol injection, usp
fresenius kabi usa, llc

supplied in single-use ampuls for intramuscular injection, containing haloperidol hydrochloride in sterile water for injection.

contraindications

a. patients with known hypersensitivity to haloperidol or other compositions (including excipients) of this product.
b. patients with a history of clinically significant leukopenia, neutropenia, agranulocytosis, thrombocytopenia, pancytopenia, aplastic anemia, or drug-induced aplastic anemia.
c. simultaneous use of antiviral agents with a significant impact on cytochrome p450 3a4 (cyp3a4) metabolism, or hormonal contraceptives.
d. patients with the potential for clinically significant organic brain syndrome or other neurological conditions.
e. patients with a history of extrapyramidal syndrome or other neuro-psychiatric disorders.
f. patients with a history of severe extrapyramidal symptoms following a previous antipsychotic drug treatment.

 WARNINGS

a. severe extrapyramidal symptoms, including neuroleptic malignant syndrome (nms), have been reported with antipsychotic drugs, including haloperidol. nms is a rare but potentially fatal syndrome characterized by a hyperthermic state, muscle rigidity, altered mental status (including catatonic signs), and autonomic instability (e.g., cardiac dysrhythmias, diaphoresis, and hypotension). it may also be associated with abnormalities in laboratory findings such as elevated serum enzymes, elevated creatine phosphokinase, hyperpyrexia, muscle rigidity, altered mental status (including catatonic signs).

b. malignant syndrome (nms) has been reported in association with antipsychotic treatment,

information for patients

a. patients receiving antipsychotic drugs should be warned of the potential for severe extrapyramidal symptoms, including neuroleptic malignant syndrome (nms), and should be informed that severe extrapyramidal symptoms, including nms, can occur among patients treated with haloperidol.

b. patients should be warned of the potential for serious adverse reactions, including extrapyramidal symptoms and neuroleptic malignant syndrome.

c. patients should be informed that haloperidol injection is available in both intramuscular and intravenous formulations.

adverse reactions

a. the most common adverse reactions associated with haloperidol injection are:

1. extrapyramidal symptoms
2. sedation
3. hyperhidrosis
4. dyskinesia
5. dystonia
6. akathisia
7. tardive dyskinesia
8. somnolence
9. diaphoresis
10. hyperpyrexia
11. muscle rigidity
12. altered mental status (including catatonic signs)
13. autonomic instability (e.g., cardiac dysrhythmias, diaphoresis, and hypotension)
14. abnormal laboratory findings such as elevated serum enzymes, elevated creatine phosphokinase, hyperpyrexia, muscle rigidity, altered mental status (including catatonic signs)

b. the incidence of these adverse reactions was determined in controlled clinical trials of 443 patients (total 10,679 days of exposure) who received haloperidol injection, usp, at doses ranging from 0.1 mg to 20 mg per day. the adverse reaction incidence rates are summarized in the following table:

<table>
<thead>
<tr>
<th>adverse reaction</th>
<th>placebo (n=16)</th>
<th>haloperidol (n=427)</th>
</tr>
</thead>
<tbody>
<tr>
<td>extrapyramidal symptoms</td>
<td>2% (2/16)</td>
<td>19% (81/427)</td>
</tr>
<tr>
<td>sedation</td>
<td>12% (2/16)</td>
<td>27% (116/427)</td>
</tr>
<tr>
<td>hyperhidrosis</td>
<td>2% (2/16)</td>
<td>13% (56/427)</td>
</tr>
<tr>
<td>dyskinesia</td>
<td>5% (1/16)</td>
<td>33% (141/427)</td>
</tr>
<tr>
<td>dystonia</td>
<td>2% (1/16)</td>
<td>12% (51/427)</td>
</tr>
<tr>
<td>akathisia</td>
<td>2% (1/16)</td>
<td>9% (39/427)</td>
</tr>
<tr>
<td>tardive dyskinesia</td>
<td>1% (1/16)</td>
<td>12% (51/427)</td>
</tr>
<tr>
<td>somnolence</td>
<td>1% (1/16)</td>
<td>7% (30/427)</td>
</tr>
<tr>
<td>diaphoresis</td>
<td>2% (1/16)</td>
<td>11% (45/427)</td>
</tr>
<tr>
<td>hyperpyrexia</td>
<td>1% (1/16)</td>
<td>5% (21/427)</td>
</tr>
<tr>
<td>muscle rigidity</td>
<td>0% (0/16)</td>
<td>2% (9/427)</td>
</tr>
<tr>
<td>altered mental status (including catatonic signs)</td>
<td>0% (0/16)</td>
<td>5% (21/427)</td>
</tr>
<tr>
<td>autonomic instability (e.g., cardiac dysrhythmias, diaphoresis, and hypotension)</td>
<td>0% (0/16)</td>
<td>5% (21/427)</td>
</tr>
<tr>
<td>abnormal laboratory findings such as elevated serum enzymes, elevated creatine phosphokinase, hyperpyrexia, muscle rigidity, altered mental status (including catatonic signs)</td>
<td>0% (0/16)</td>
<td>5% (21/427)</td>
</tr>
</tbody>
</table>

cases of sudden death, QT-prolongation, and torsades de pointes have been reported with antipsychotic treatment.

no association has been established between QT-prolongation and torsades de pointes.

other adverse reactions

a. other adverse reactions that have been reported with haloperidol injection include:

1. extrapyramidal symptoms
2. sedation
3. hyperhidrosis
4. dyskinesia
5. dystonia
6. akathisia
7. tardive dyskinesia
8. somnolence
9. diaphoresis
10. hyperpyrexia
11. muscle rigidity
12. altered mental status (including catatonic signs)
13. autonomic instability (e.g., cardiac dysrhythmias, diaphoresis, and hypotension)
14. abnormal laboratory findings such as elevated serum enzymes, elevated creatine phosphokinase, hyperpyrexia, muscle rigidity, altered mental status (including catatonic signs)

caution

a. patients receiving haloperidol injection should be monitored closely for early evidence of neurological toxicity and treatment withdrawn. antipsychotic treatment, itself, however, may suppress (or partially suppress) extrapyramidal symptoms and thereby mask the emergence of drug-induced parkinsonism.

b. patients receiving haloperidol injection should be monitored closely for cardiac dysrhythmias.

c. if torsades de pointes occurs, haloperidol injection should be withdrawn immediately.

d. cases of sudden death, QT-prolongation, and torsades de pointes have been reported with antipsychotic treatment. no association has been established between QT-prolongation and torsades de pointes.

e. when prolonged treatment (1-2 weeks) with enzyme-inducing drugs such as rifampin or carbamazepine is administered or discontinued in haloperidol-treated patients, the a mean 3.3-fold increase in haloperidol concentrations may be observed.

f. haloperidol is metabolized by several routes, including the glucuronidation and catalytic oxidation.

g. other drugs that may affect haloperidol metabolism include:

1. anticholinergic agents
2. other antipsychotic agents
3. anti-convulsant medications
4. other drugs known to induce cyp3a4

administration

a. haloperidol injection is indicated for oral administration for the treatment of acute and chronic psychotic disorders including schizophrenia.

b. haloperidol injection is also indicated for the treatment of acute exacerbations of chronic psychotic disorders, including schizoaffective disorders and delusional disorders.

patients with a history of a clinically significant low wbc or a drug-induced aplastic anemia should be monitored closely for early evidence of hematological toxicity and treatment withdrawn. antipsychotic treatment, itself, however, may suppress (or partially suppress) hematopoiesis, and thereby mask the emergence of drug-induced thrombocytopenia.

sodium valproate, a drug known to inhibit glucuronidation, does not affect the pharmacokinetic profile of haloperidol.